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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,656	12/12/2001	Keith D. Allen	R-390	3892

26519 7590 01/20/2011

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
01/20/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/016,656	ALLEN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7-28-04 & 9-28-04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9 and 14-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-9 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ___.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The petition to withdrawn the abandonment filed 7-28-04 was granted on 9-28-04. The office action sent 11-6-03 has been vacated in favor of the instant office action.

The amendment to the description of Fig. 2A-2B has been entered. However, the description remains unclear. The description should include the fact that Fig. 2A-2B shows the GPRC5B-like gene (SEQ ID NO:1). Correction is required.

Election/Restrictions

Applicant's election without traverse of Group II, claims 3-9 and 14-18, is acknowledged.

Claims 1, 2, 10-13 and 19-30 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claim Objections

Claim 9 is objected to because it is dependent upon claim 1 which is not under consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-9 and 14-18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

Claims 6, 7 and 14-17 are directed toward a transgenic animal having a disruption of a GPRC5B-like gene and abnormal pain threshold. The specification teaches making GPRC5B-like -/- mice (pg 52). The specification suggests using the mice as a model of disease, specifically as a model for behavioral, neurological, psychoneurological, psychotic phenotypes, and increased pain threshold (pg 19-21; pg 21, lines 9-16). However, the specification does not disclose one specific behavioral, neurological, neuropsychological or psychotic disease or disease related to increased pain threshold in humans linked to a disruption in GPRC5B-like. The mice were tested in a "hot plate test" (pg 54). GPRC5B-like -/- mice had an increased pain threshold as compared to wild-type. However, the results of the hot plate test do not correlate to a useful phenotype because an increased pain threshold is not specific to a disease linked to a disruption in a GPRC5B-like gene. The results are not statistically significant because the number of mice tested is not disclosed. The mice claimed cannot be used to determine compounds that modulate GPRC5B-like expression (e.g. claim 10, not under consideration) because GPRC5B-like is not expressed in the mice. Using the mice to determining whether a particular phenotype is ameliorated is not a specific or substantial utility because the specification does not link the phenotype to any specific disease or to a disease caused by a disruption in humans. The specification does not identify any compounds that alter neurological, neuropsychological, or psychotic

phenotypes using the mice. Thus, the specification does not provide a specific or substantial use for a mouse having abnormal pain threshold or increased latency to lick a hind paw in response to a hot plate in a hot plate test as claimed.

Claim 9 is included because it is directed toward making the mouse, which lacks utility for reasons above. Claims 3-5, 8 and 18 are directed toward cells having a disruption of a GPRC5B-like gene or a cell derived from the transgenic animal, and are included because the cells lack a specific and substantial utility for the reasons above and because the specification does not teach how to use the cells other than when they are part of a mouse that is a model of disease.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-9 and 14-18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use mice having abnormal pain threshold.

The specification does not teach how to make animals or cells having a disruption in a GPRC5B-like gene other than mice (claims 3-5, 8 and 18). Specifically,

claims 4-5 encompass mice and rat cells. "Murine" encompasses mice and rats (http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=murine). The only means of making a cell with a disruption in a GPRC5B-like gene taught in the specification is by using mouse embryonic stem cell technology. The state of the art at the time of filing was such that embryonic stem (ES) cell technology had only been successful in mice. Wagner (May 1995, Clin. and Experimental Hypertension, Vol. 17, pages 593-605) and Mullins (1996, J. Clin. Invest., Vol. 98, pages 1557-1560) taught germline transmission of ES cells has not been demonstrated in species other than mice and the growth of ES cells from species other than mice is unreliable. Wall (1996, Theriogenology, Vol. 45, pg 57-68) taught transgene expression and the physiological result of such expression in livestock was not always accurately predicted in transgenic mice (page 62, line 7). The specification fails to provide sufficient guidance to make transgenics other than mice by teaching obtaining ES cells in species other than mice. The specification does not teach the nucleic acid sequence of a GPRC5B-like gene in non-mice, non-human species or correlate the GPRC5B-like gene in mice to the GPRC5B-like gene in other species. The specification does not teach how to make knockout animals other than mice or correlate making knockout mice to other species. Therefore, the specification does not provide adequate guidance for one of skill in the art to make a transgenic, non-human animal or cells having a disruption in a GPRC5B-like gene in any species other than mice.

The specification does not provide adequate correlation between the phenotype obtained in mice to the phenotype obtained in other species. The state of the art at the

time of filing was that the phenotype of transgenic mice does not predict the phenotype in non-mice species. Models of human diseases have relied on transgenic rats when the development of transgenic mice having the desired phenotype was not feasible. Mullins (1990, Nature, Vol. 344, pg 541-544) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse Ren-2 renin transgene. Hammer (1990, Cell, Vol. 63, pg 1099-1112) describes spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human b_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice (Mullins, 1989, EMBO, Vol. 8, pg 4065-4072; Taurog, 1988, J. Immunol., Vol. 141, pg 4020-4023) expressing the same transgenes that successfully caused the desired symptoms in transgenic rats. Therefore, the specification does not enable making transgenic having the disclosed phenotypes in species other than mice.

In addition, claims 14-17 do not provide a nexus between the disruption in GPRC5B-like and the lack of production of GPRC5B-like or the phenotypes claimed. The claims do not recite the disruption of GPRC5B-like causes the phenotype claimed. The specification does not teach disrupting the GPRC5B-like gene in mice already lacking production of GPRC5B-like or in mice already having abnormal pain thresholds. Given the art of transgenics at the time of filing taken with the guidance provided in the specification, the claim should reflect the fact that mice having abnormal pain threshold is a result of GPRC5B-like disruption. Otherwise, it would require one of skill undue experimentation to make the mouse as broadly claimed.

The specification does not enable making or using a transgenic with a wild-type phenotype as encompassed by the claims. The transgenics of claims 6, 7, 9 and 14 do not recite any phenotype and may, therefore, have any phenotype including wild-type phenotype. The specification does not provide any use for a transgenic having a disruption in a GPRC5B-like gene that has a wild-type phenotype. The only disclosed phenotype for the transgenic claimed is one that correlates to a mutation in a GPRC5B-like gene. Therefore, the claims should recite a non-wild-type phenotype that correlates to a disruption in a GPRC5B-like gene.

Claim 9 is directed toward a method of making a transgenic mouse having a disruption in GPRC5B-like using a mouse ES cell having a disruption in an endogenous GPRC5B-like gene, introducing the cell into a mouse blastocyst, implanting the blastocyst into a pseudopregnant mouse which gives birth to chimeric mice, and breeding the chimeric mouse to produce the transgenic mouse. The claim does not require using mouse cells or an embryonic stem cell, which are considered essential to the invention. A mouse ES cell is the only type of cell taught in the specification that can be introduced into a blastocyst and result in a chimeric mouse as claimed. The claim does not require the mouse have a non-wild type phenotype, which is required for reasons cited above. Given the unpredictability in the art taken with the guidance provided in the specification, the cell in a) should be a mouse ES cell, the blastocyst in b) should be a mouse blastocyst, and the transgenic mouse produced should have a genome comprising a homozygous disruption in a GPRC5B-like gene, wherein said mouse lacks functional GPRC5B-like protein and has a disclosed phenotype.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-9 and 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of what applicants consider "GPRC5B-like" genes cannot be determined. The specification defines the term as any gene of SEQ ID NO:1 or having homology to SEQ ID NO:1 (pg 7, lines 6-17). However, not all genes sharing homology with SEQ ID NO:1 are GPRC5-like genes. For example, other GPCR genes share homology with SEQ ID NO:1, but are not GPRC5B genes.

Claims 14-17 are indefinite because they do not clearly set forth that the disruption in GPRC5B-like causes the lack of production of GPRC5B-like or an abnormal pain threshold.

The metes and bounds of what applicants consider "significant" expression (claim 14) cannot be determined.

The metes and bounds of what applicants consider "abnormal" pain threshold (claim 15) cannot be determined. The term is relative and is not defined in the specification.

The term "characterized" in claim 17 is unclear. It cannot be determined if the claim is limited to the phenotype recited or if the claim encompasses mice having a phenotype related to the phenotype recited.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday through Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner